Voluntariness of Consent to Research:
A Preliminary Empirical Investigation

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Providing informed consent to participate in research—a primary pillar of the ethical conduct of research—is based on three components: *adequate information*, a *competent decision-maker*, and a *voluntary decision process*.[1] Techniques have been developed to assess the content and adequacy of information disclosures during the informed consent process[2] and the decisional capacity of people recruited to participate in research.[3] But voluntariness of consent has been more resistant to investigation, leaving policy-makers with little guidance for their efforts to insure that prospective research subjects are able to exercise meaningful choice about whether to participate in research.

Notwithstanding the paucity of empirical data, a considerable amount of regulation aimed at promoting voluntary choice has been promulgated in response to concerns over possible coercive influences in recruitment for research studies.[4] In addition, many IRBs have developed internal policies, e.g., limiting the incentives that can be provided to research subjects[5] or precluding recruitment of patients without their physician's approval. Given that additional protections can impede recruitment and/or raise its costs—and that the populations affected by these protections are often among those for whom the knowledge base is smallest and the concomitant need for research particularly great—it is important to know to what extent current approaches are successful in mitigating the problem.

All tables referred to in this article can be found at http://www.thehastingscenter.org/Publications/IRB.

Existing data, however, are of limited utility for that purpose. Studies focus largely on two populations: subjects who receive financial incentives and research participants in studies in the developing world. Minimal information is available regarding other categories of subjects.[6]

Offering financial incentives to participate in research has raised concerns that compensation might unduly influence people's decisions about whether to enroll in research, leading them to disregard the potential risks of participation.[7] Studies of decision-making using hypothetical research protocols suggest that incentives can influence decisions, but that they generally do not lead people to ignore research risks.[8] The only *in vivo* studies of which we are aware examined the impact of varying levels of payment on substance abusers' attendance at follow-up sessions; higher levels of payment were associated with better attendance, without greater perceived coercion or drug use.[9]

Populations in developing countries are often thought to be subject to a variety of coercive influences, ranging from pressures exerted by authority figures to difficulty understanding that research participation is voluntary.[10] For instance, in studies conducted in Africa and Asia, many people said they did not perceive that they were free to make decisions about research participation or to withdraw from a study in which they were enrolled.[11] However, studies that asked directly about the sources of such pressure revealed that people infrequently attributed these influences to the researchers' themselves,[12] leaving open the question of how such effects could be mitigated.

Interpretation of the studies conducted in developing countries about issues related to financial incentives is complicated by the variety of assessment approaches that have been used, making it difficult to compare data across studies. The studies were often based on a single question and nearly all focused on a single subject population, usually with a constricted range of independent variables. These limitations hamper efforts to identify predictors of diminished voluntariness as well as motives for participating in research.

Given the absence of accepted measures of voluntariness in research settings and the limited amount of available data, our study was designed to develop a more comprehensive approach to assessing voluntariness of consent to research and to generate preliminary data on the extent and correlates of limitations on voluntariness across diverse areas of research.

Study Methods

The individuals recruited for this study had previously agreed to

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participate in a clinical trial (referred to in this report as their "primary study") at a major university medical center in one of five areas of research: substance abuse, cancer, HIV, interventional cardiology, or depression. After giving informed consent for their primary study, they were asked by research staff for that study if they would be willing to be contacted about participating in this additional study of voluntariness. Those who responded affirmatively were contacted in person or by telephone, given information about the study, and offered $20 for their participation. Distribution of participants in our study by category of research is shown in Table 1. Because of the method of recruitment, we cannot know the number of potential participants who were not asked about being contacted, or who declined to be approached.

Instrument development began with an initial conceptualization of potential limitations on voluntariness, based on a model of voluntary decision-making rooted in the law of informed consent.[13] The premise underlying the law's approach to voluntariness is that although all decisions are susceptible to multiple influences, voluntary decisions should reflect the will of the decision-maker rather than of another person. This is shown in the legal rule that consent is ineffective if given under duress. Influences that may render decisions involuntary share a common set of characteristics: they are *external*, *intentional*, *illegitimate*, and *causally linked* to the choice of the person participating in research.[14] Drawing on the work of sociologist Talcott Parsons, who conceptualized the mechanisms by which one person can exert influence on the decisions of another,[15] we identified *offers*, *pressures*, or *threats* related to research participation as those types of influence most likely to meet these criteria. Interviews were then conducted with 15 research staff members who routinely obtain consent from individuals willing to enroll in research about the offers, pressures, and threats that they observed in the research setting to discover their views on individuals' motivations for agreeing to provide consent. We also conducted interviews with 19 recently recruited research subjects from a variety of research projects who were asked a parallel set of questions. The interviews were digitally recorded, transcribed, and summarized to highlight key aspects of participants' responses.

Based on the information obtained in these interviews—which suggested that a broad understanding of motivations is required to assess the extent to which research subjects' voluntariness may be limited—we developed a questionnaire that addressed three areas: demographic data, motivations for participating in research, and experience of offers, pressures, or threats. The questionnaire asked respondents to choose from among 14 possible motivations for enrolling in research (see Table 2). If they identified a motivation as having played some role in their decisions, they were to indicate on a scale of one to 10 the degree of influence associated with that motivation. They were then asked separately whether they had been subject to offers, pressures, and threats, and if so, to describe 1) what happened, 2) the extent to which it influenced their decisions, and 3) the degree to which they considered the offer, pressure, or threat to have been unfair (again on scales of one to 10). We also asked respondents about the risks they perceived were associated with the primary study and the role of offers, pressures, or threats in making the risks worth accepting. Finally, respondents completed a modified version of the MacArthur Perceived Coercion Scale[16] and a modification of the Coercion Ladder[17] that we refer to as the Voluntariness Ladder. These instruments are previously published measures of voluntariness of decisions in treatment contexts.

We identified *offers*, *pressures*, or *threats* related to research participation as the types of influence most likely to reflect mechanisms by which one person can exert influence on the decisions of another.

This study was approved by the institutional review board (IRB) of the New York State Psychiatric Institute, and participants gave written informed consent. We interviewed 88 participants a median of three weeks after they consented to participate in their primary study (in all cases a clinical trial) (mean: 4.6 +/– 4.8 weeks). Interviews were conducted by a trained research assistant, were digitally recorded for purposes of analysis, and took approximately one-half hour to complete.

Study Findings

Table 3 provides descriptive characteristics of the 88 respondents. Of particular note, roughly one-third had participated in clinical research prior to being recruited for their primary study; this figure is substantially greater than the approximately 10% of adults in the United States who report having participated in a clinical research study[18] but could be expected to be elevated among a group of current research participants.

The number of respondents endorsing each of 14 possible motivations for research participation, and the extent to which their ratings of importance (on a one to 10 scale) tended to cluster in the upper or lower range of the scale are shown in Table 2. The possibility of better care, trust in the people doing the research, and the reputation of the host institutions were frequently cited as important motivations

across all categories of respondents. However, some differences could be identified across the various respondent groups. Comparing the importance of the motivation variables among respondents who were participating in oncology, substance abuse, and other clinical trials, significant differences exist for the availability of free treatment (ANOVA, df = 83, F = 14.41, p < 0.0001; substance abuse highest and oncology lowest); how seriously respondents needed help for their condition (ANOVA, df = 84, F = 5.07, p < 0.01; substance abuse highest and oncology lowest); advice from their doctors or nurses (ANOVA, df = 86, F = 19.56, p < 0.0001; oncology highest and substance abuse lowest); and desire to help others with the same medical condition (ANOVA, df = 85, F = 5.22, p = .0073; oncology highest and substance abuse lowest). Respondents who were enrolled in substance abuse trials placed less emphasis on altruism as a motivation for participation and more on the availability of free treatment and the seriousness of their need for treatment. On the other hand, respondents in oncology trials—who are faced with life-threatening illnesses—placed the greatest weight of the three respondent groups on advice from their medical caregivers. No one pattern of motivation to enroll in a trial appeared to be characteristic of all the areas of clinical research examined in this study.

A factor analysis of possible motivations that were endorsed by more than a small number of respondents was performed, using a principal components analysis and a varimax rotation that yielded two factors, as demonstrated in Table 4. The first factor, which we label "Help and Trust," drew most heavily on the possibility of getting better care, access to treatment not otherwise available, how seriously help was needed, trust in the people doing the research study, and the reputation of the institution. The second factor, which we call "Free Treatment," was based primarily on the availability of free treatment, not getting advice from a doctor or nurse, and not having altruistic motivations. Although there were no significant differences in the distribution of the first factor among the three types of research (ANOVA, df = 60, F = 0.25, p = 0.78), the second factor did differ significantly, being strongest for respondents who participated in the substance abuse studies and weakest for those in the oncology trials (ANOVA, df = 60, F = 18.73, p < 0.0001).

Constraints on Voluntariness. Offers tied to research participation were reported by 31 respondents (35%), pressures by three (3%), and threats by none. Most respondents who reported offers rated them as having had little importance in their decision-making (26 of 31 respondents assigned an importance rating in the lower half of the one to 10 scale, with 19 of those giving it the lowest possible score). Only one respondent assigned the offer an importance of 10 out of 10. Of the three respondents who reported pressures, none rated the importance of the pressure in the upper half of the scale.

Respondents also completed two global measures of voluntariness: the Perceived Coercion Scale and the Voluntariness Ladder. Scores on the Perceived Coercion Scale ranged from zero to five, based on true/false responses to five questions, with higher numbers indicating increased perceptions of coercion. Scores were available for 86 respondents; of those, 65 respondents had a score of zero, 18 had a score of one, and three had a score of two. Most of the positive indicators of coercion (18 of 25) came from a single question (True/False: "It was my idea to sign up for the research project"), which may have been interpreted merely as inquiring about the source of a suggestion about participation, and thus may not be an accurate indicator of constrained volition. Thus, there was very little evidence from the Perceived Coercion Scale that respondents perceived their decisions as having been coerced in any way. Confirmatory evidence comes from the data generated by the Voluntariness Ladder, a simple measure that asks subjects to rate how voluntary their decision was on a one to 10 "Ladder," with one indicating a choice that is not at all voluntary and 10 a completely voluntary choice. Of the 85 respondents for whom data were available, 73 rated their decisions as completely voluntary and only one assigned a rating in the lower half of the scale (i.e., a score of five out of 10). Scores for the Perceived Coercion Scale and the Voluntariness Ladder were moderately but significantly correlated (r = 0.38, p = 0.0003), though neither score was predicted by any of the descriptive variables.

Relationships between the Perceived Coercion Scale and Voluntariness Ladder scores, respectively, and motivations for participation were significant in a small number of cases. Higher scores on the Perceived Coercion Scale (i.e., greater perceived coercion) were associated with greater importance of helping others as a motivation for research participation (ANOVA, df = 85, F = 4.6, p = 0.03), and increased importance of an offer in the decision (ANOVA, df = 85, F = 5.27, p = 0.02). They were also associated with higher ratings of the importance of "advice from your doctor or nurse" (ANOVA, df = 84, F = 5.33, p = 0.02), but this association may be due to the previously noted ambiguity in the scale's question regarding the source of the idea for research participation. None of these variables, however, was significantly associated with scores on the Voluntariness Ladder.

Discussion

This study's approach to assessing voluntariness involved a set of

questions aimed at directly ascertaining respondents' views regarding the presence and importance of offers, pressures, and threats—along with two global measures of perceived coercion/voluntariness—to their decisions about research participation. To obtain a more complete picture of decision-making, we also took into account the positive motivations for enrolling in research and the importance of these considerations.

Taken as a whole our data suggest that individuals have diverse reasons for wanting to participate in research, and that—consistent with the existing literature on research subjects' motivations[19]—their decisions are usually driven by more than one consideration. For example, respondents indicated that the need for help with a significant medical condition or the desire for a higher level of care was frequently combined with a high degree of trust in the investigator and institution as factors that contributed to their decision to participate in research; this association existed regardless of the medical condition for which they sought an intervention by enrolling in a clinical trial. However, there was systematic variation in other motivations by the nature of the condition and the intervention being studied. For instance, for respondents who participated in substance abuse trials, decisions seem to have been driven most strongly by the availability of free care—not usually conceived of as an incentive, but perhaps reasonably understood in this way.

Notably, in this sample of clinical trials from diverse areas of medicine there was little evidence of constraints on voluntariness, and when such influences were present they almost never were reported as having played a significant role in individuals' decisions. Specifically, although offers were common, they rarely were perceived as playing a major role in the decision-making process. Even if they had, we would still need to inquire whether they led individuals to undervalue or ignore significant research-related risks before we concluded there was reason for concern. These findings are consistent with a growing body of literature from both empirical and theoretical perspectives suggesting that the potential for incentives to act as constraints on voluntariness has been overrated.[20] Only three respondents reported pressures placed on them by other people to enroll in a research study or to forgo participation, and none of the pressures reached a level of importance that appeared to have materially influenced their decisions. No respondents reported receiving overt threats.

Our findings reveal little evidence of constraints on voluntariness, and when such influences were present they did not play a significant role in individuals' decision-making process.

Although these data are reassuring with regard to the degree of voluntariness of decisions to enter clinical trials, they provide some hints of areas that might warrant further exploration regarding their influence on voluntary decision-making. Offers to prospective research subjects—usually direct financial compensation—have been a focus of concern for IRBs and research regulators for many years, and the data here concerning their impact on voluntariness were somewhat equivocal. Although the presence of an offer was associated with significantly lower scores on the Perceived Coercion Scale (i.e., less perceived coercion), scores rose as the importance of the offer to the individual's decision-making increased. Paradoxically, higher scores on the Perceived Coercion Scale were also associated with the greater importance of helping others—i.e., altruism—in individuals' decision-making. One explanation for this is that individuals who feel "compelled" to help others, for moral or personal reasons, perceive themselves as less free to turn down the opportunity to participate in a clinical trial. Whether that phenomenon, if confirmed, should be of concern to policy-makers and ethicists is unclear, since altruism is generally regarded as the least problematic motivation for participation in research. Finally, when advice from physicians or nurses played a more important role in decision-making, respondents tended to have higher scores on the Perceived Coercion Scale, suggesting that this source of advice may leave individuals feeling less free to say no; however, since the relevant question on the scale is susceptible to differing interpretations, this finding is in need of confirmation using alternative approaches.

These data, of course, have limitations that should be underscored. They are derived from a newly developed (though we would argue face-valid) conceptualization of voluntariness and its constraints[21] and a previously untested approach to assessment. Moreover, they reflect the experiences of a relatively small number of individuals who participated in a limited group of clinical trials at a single academic medical center. An additional limitation inherent in the approach taken here is that our assessment of constraints on voluntariness was based on the reports of research subjects themselves, both with regard to their specific experiences and the degree to which their decisions were constrained. Insofar as they may have failed to recognize or report the presence or impact of a problematic influence on their decisions, we would not have been able to detect it here. However, this is a limitation with which the field of research ethics may need to live for now, because—outside of an experimental setting—it does not appear feasible to assess influences on individuals'

decision-making other than from the perspective of the individuals themselves.

Thus, although these data in themselves offer no reasons for concern about constraints on voluntariness regarding decisions about research participation, we caution against relying on the data for purposes other than the design of further research in this area. Such future research might usefully aim at validating assumptions prevailing in existing regulations and policies regarding groups at heightened risk of impaired voluntariness; identifying approaches to recruitment that can impair voluntariness (e.g., substantial incentives); and developing methods of reducing the possibility that individuals may not be able to make an adequately voluntary decision about research participation.

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